ADENOSINE MONOPHOSPHATE-ACTIVATED PROTEIN KINASE ATTENUATES CARDIOMYOCYTE HYPERTROPHY THROUGH REGULATION OF FOXO3A/MAFBX SIGNALLING PATHWAY

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Aim To examine the inhibitory effects of adenosine monophosphate-activated protein kinase (AMPK) activation on cardiomyocytes hypertrophy and explore the underlying molecular mechanisms.

Methods Cultured neonatal rat cardiomyocytes were treated with specific AMPK activator 5-aminoimidazole-4-carboxamide ribonucleoside (AICAR) and AMPK antagonist Compound C, and stimulated with angiotensin (Ang). The muscle atrophy F-box (MAFbx)-small interfering RNA (siRNA) was transfected into cultured cardiomyocytes by Lipofectamine 2000. The surface area of cell was measured by planimetry. The expression of ANP, BNP and MAFbx, as well as the phosphorylation levels of AMPK and Forkhead box O 3a (FOXO3a) were measured by western blot or RT-PCR, separately.

Results Activation of AMPK by AICAR inhibited Ang II-induced increase in cardiomyocyte area, as well as ANP and BNP protein expression. Furthermore, AMPK activation increased the activity of transcription factor FOXO3a and up-regulated downstream atrogene MAFbx mRNA and protein expression. Treatment of hypertrophied cardiomyocytes with Compound C blocked the effects of AMPK on cardiomyocytes hypertrophy and changes in the FOXO3a/MAFbx signalling pathway. The effects of AICAR on cardiomyocytes hypertrophy were also blunted after MAFbx was silenced by transfection of cardiomyocytes with MAFbx-siRNA.

Conclusion Our results indicate that AMPK plays an important role in the inhibition of cardiomyocyte hypertrophy by activating protein degradation via FOXO3a/MAFbx signaling pathway.